376. *Pyridine-4-sulphonic Acid.*

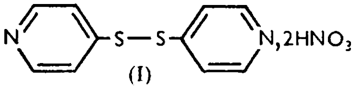
By A. M. Comrie and J. B. Stenlake.

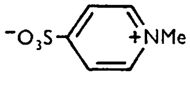
The substance prepared by nitric acid oxidation of 4-thiopyridone and previously described as pyridine-4-sulphonic acid is shown to be a mixture of pyridine-4-sulphonic acid and di-4-pyridyl disulphide dinitrate. Pyridine-4-sulphonic acid can be prepared by oxidation of 4-thiopyridone with hydrogen peroxide in glacial acetic acid.

Koenigs and Kinne [1] oxidised 4-thiopyridone with nitric acid to an acid of m. p. 134—135° which they regarded as pyridine-4-sulphonic acid, and, in support of this structure, cited an analysis and preparation of a barium and a silver salt. King and Ware,[2] similarly, oxidised 4-thiopyridone, but with alkaline hydrogen peroxide, and obtained sodium pyridine-4-sulphonate. Neither from this salt nor from 4-thiopyridone could they prepare pyridine-4-sulphonyl chloride or the amide.

We have now oxidised 4-thiopyridone by hydrogen peroxide in glacial acetic acid and obtained an acid, $C_5H_5O_3NS$, of m. p. 333° which, as it was also prepared by passing a solution of sodium pyridine-4-sulphonate [2] through a cation-exchange resin, is undoubtedly pyridine-4-sulphonic acid. This was confirmed by potentiometric titration with sodium hydroxide (which gave a curve typical of that of a strong acid) and by analysis of the ammonium salt. Further, the high m. p. and the failure to form a picrate accord with the expected zwitterionic structure.

Repetition of Koenigs and Kinne's work [1] gave an acidic product of m. p. 135° which was separated by fractional crystallisation into pyridine-4-sulphonic acid, identical with that described above, and a larger proportion of a more soluble substance, m. p. 127°. The latter was readily soluble in water, giving a strongly acid solution, and titrated potentiometrically as a strong acid (equiv., 174). It was identified as di-4-pyridyl disulphide dinitrate (I) by elementary analysis and by isolation of the corresponding base, identical with authentic material [2] (see below). The base picrate was identical (m. p. and crystal form) with di-4-pyridyl disulphide dipicrate. Preparation of the platinichloride [1] and oxidation with hydrogen peroxide in acetic acid to pyridine-4-sulphonic acid confirmed the identity of the base. The nitrate radical was established qualitatively (brown-ring test) and quantitatively (determination of the ammonia produced on reduction with Devarda's alloy).


(I)


(II)

The m. p. of the di-4-pyridyl disulphide has been variously reported as 155° [1] and 74°.[2] The material isolated as above from the dinitrate (I) melted at 74°. Disulphide prepared as described by Koenigs and Kinne [1] also melted at 74°. This with dilute nitric acid gave di-4-pyridyl disulphide dinitrate (I) identical with that obtained from 4-thiopyridone. Attempts to esterify pyridine-4-sulphonic acid by hydrogen chloride–ethanol,[3] trifluoroacetic anhydride–ethanol,[4] and dimethyl sulphate were unsuccessful. Treatment of the acid with diazomethane in presence of traces of water [5] gave the corresponding betaine (II), apparently identical (but with some discrepancy in m. p.) with that obtained by heating sodium pyridine-4-sulphonate with dimethyl sulphate.[6]

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[1] Koenigs and Kinne, *Ber.*, 1921, **54**, 1357.
[2] King and Ware, *J.*, 1939, 873.
[3] U.S.P. 2,349,060 (1944).
[4] Bourne, Stacey, Tatlow, and Tedder, *J.*, 1949, 2976.
[5] Biltz, *Ber.*, 1922, **55**, 1066.
[6] Larivé, Collet, and Dennilauber, *Bull. Soc. chim. France*, 1956, 1443.

EXPERIMENTAL

4-Thiopyridone was prepared from chelidonic acid [7] as described by King and Ware.[2]

Pyridine-4-sulphonic Acid.—(*a*) 4-Thiopyridone (0·5 g.), in glacial acetic acid (10 ml.) and 30% hydrogen peroxide (1·6 ml.), was heated on a water-bath for ½ hr. Acetic acid was removed under reduced pressure. The residue recrystallised from aqueous methanol (charcoal) in colourless plates (0·25 g., 36%) of *pyridine-4-sulphonic acid*, m. p. 333° (decomp.) [Found: C, 37·5; H, 3·0; N, 8·8%; equiv. (potentiometric titration), 160. $C_5H_5O_3NS$ requires C, 37·7; H, 3·1; N, 8·8%; equiv., 159].

(*b*) Sodium pyridine-4-sulphonate, prepared as described by King and Ware,[2] was dissolved in water, and the solution passed through a column of Zeo-Karb 225. The eluate, evaporated to dryness, gave pyridine-4-sulphonic acid, m. p. 333—334° (decomp.) (from ethanol–water), identical with that obtained as in method (*a*). The *ammonium salt* separated from aqueous methanol at 0° as a colourless solid, m. p. 256° (decomp.) (Found: N, 16·2. $C_5H_8O_3N_2S$ requires N, 15·9%).

(*c*) Di-4-pyridyl disulphide (0·5 g.), treated as in (*a*) for the acid, yielded pyridine-4-sulphonic acid, m. p. 333° (from aqueous methanol), identical with that obtained as in method (*a*).

Oxidation of 4-Thiopyridone with Nitric Acid.—4-Thiopyridone (2 g.) was heated on a water-bath with nitric acid (*d* 1·2; 20 ml.) until vigorous reaction commenced (*ca.* 5 min.). After the reaction had subsided the solution was evaporated to dryness. The residue (3·3 g.), recrystallised from water (8 ml.), gave pale yellow needles of *di-4-pyridyl disulphide dinitrate* (1·8 g., 58%) which, after being washed with ice-cold water (2 ml.) and dried *in vacuo*, had m. p. 127° (decomp.) [Found: C, 35·0; H, 2·5: N, 15·8; Nitrate-N (determined by reduction with Devarda's alloy in a Conway cell and titration of the liberated ammonia), 8·0, 8·2. $C_{10}H_{10}O_6N_4S_2$ requires C, 34·7; H, 2·9; N, 16·2; Nitrate-N, 8·1%].

The combined mother-liquors and washings, treated with ethanol (40 ml.), deposited a crystalline solid, m. p. 135° (decomp.) (1·1 g.); recrystallisation from aqueous ethanol gave colourless plates of pyridine-4-sulphonic acid (0·53 g.), m. p. 333—334° (decomp.), identical with authentic material. The filtrate was evaporated to dryness and the residue recrystallised from 90% ethanol (22 ml.), affording a further yield of pyridine-4-sulphonic acid (0·41 g.) (total yield 27%) (Found: C, 37·6; H, 3·0%; equiv., 158).

Di-4-pyridyl Disulphide.—Di-4-pyridyl disulphide dinitrate (0·4 g.) was treated with dilute aqueous ammonia and extracted with ether. The ethereal solution, washed with water, dried (Na_2SO_4), and evaporated, gave di-4-pyridyl disulphide (0·26 g., 96%), m. p. 75—76°. King and Ware [1] gave m. p. 74—75°. Disulphide prepared by oxidation of 4-thiopyridone in sodium hydroxide as described by Koenigs and Kinne [1] had m. p. 74—75° (Found: C, 54·4; H, 3·4. Calc. for $C_{10}H_8N_2S_2$: C, 54·5; H, 3·7%). The dipicrate (from methanol) had m. p. 230° (decomp.) (lit.,[2] m. p. 231°) (Found: C, 39·2; H, 1·9; S, 9·6. Calc. for $C_{22}H_{14}O_{14}N_8S_2$ requires C, 38·9; H, 2·1; S, 9·4%). The platinichloride formed golden-yellow plates, which decomposed about 285° (Koenigs and Kinne [1] report decomposition without melting at 275°) (Found: C, 18·7; H, 1·6; Pt, 31·0. Calc. for $C_{10}H_{10}N_2Cl_6S_2Pt$: C, 19·1; H, 1·6; Pt, 30·95%).

N-*Methyl-4-sulphopyridine Betaine.*—Pyridine-4-sulphonic acid (0·32 g.) was suspended in ether (10 ml.) and treated with excess of diazomethane. A few drops of water were added as catalyst. The reddish-brown precipitate, recrystallised from aqueous ethanol, gave the betaine (0·19 g., 54%) as colourless crystals, decomp. 330° (Found: C, 41·6; H, 3·6; N, 7·8. Calc. for $C_6H_7O_3NS$: C, 41·6; H, 4·1; N, 8·1%). Larivé *et al.*[6] report decomposition at 340° and 345°.

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[7] *Org. Synth.*, 1937, **17**, 40.